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Biomedical Lessons From the Chernobyl Nuclear Power Plant Accident

Lt Col Doris Browne, MC*

The Chernobyl nuclear accident afforded the treating physicians a chance to observe clinical ARS in man, defining the degree of severity according to average radiation dose exposure, and to make prognoses for the individual patients on the course of the ARS, based on biological criteria. The author gives a detailed account of the clinical cause of the disease including all available laboratory values. She provides valuable data that can be utilized in handling similar accidents in the future.

The world's worst radiation accident occurred at the Chernobyl nuclear power plant in the USSR during the early hours of April 26, 1986. This accident unleashed megacuries of radioactive contamination into the atmosphere, generated an explosive blast that knocked the thousand-ton lid off the top of the reactor, and sent burning graphite and heat in a plume about three miles high. The aftermath and significance of this disaster are still being realized in the USSR and neighboring countries.

Details of the accident were reported at the International Atomic Energy Agency (IAEA) meeting held in Vienna, Austria, in August 1986, and summarized in IAEA Safety Series Technic·' Report No. 75.[1,2] This report summarizes the basic information on casualties, triage, and treatment, and the radionuclides released into the atmosphere. The immediate casualties included only plant personnel, firemen, and auxiliary staff present at, or in the vicinity of the accident site.

These casualties were all subject to the combined effects of the following: short-term beta/gamma radiation released in the emission cloud; external beta/gamma radiation from fragments of the damaged reactor core scattered through the accident site; inhalation of gaseous and aerosolized dust composed primarily of radioisotopes of cesium, plutonium, and iodine; and beta/gamma particles deposited on the skin and mucous membranes from the molten steam and dust. Wet clothing contaminated by the steam and dust provided another source of contamination.

Within 15 minutes of the acident, first aid was provided by middle level medical personnel and emergency team members. Individuals with acute symptoms were transported to the hospital in Pripyat, where the initial screening took place; others in satisfactory condition were instructed to go to the hospital for examination. The initial care consisted of antiemetics, symptomatic medication, and stable saturated potassium iodide. The specialized emergency team of radiation accident specialists arrived at the accident site within 12 hours and, with the on-site medical personnel, screened and triaged more than 350 persons within the first 36 hours. During the first 24 hours, 132 persons were hospitalized; one individual died from severe thermal burns during the first hour, and another worker (a reactor operator) was unaccounted for and believed to be buried under the collapsed debris.

The triage officer, a physician, made decisions based on the initial symptoms and lymphocyte counts. Persons with severe symptoms were hospitalized with clinical complaints of acute radiation sickness (ARS). Three hundred of these patients were sent to a specialized treatment center in Moscow and another 200 were sent to a hospital in Kiev. The 237 hospitalized individuals received significant combined radiation effects from the extensive beta/gamma exposure, which was generally external and relatively uniform over the whole body, as well as with the intake of additional radionuclides through inhalation. These patients were diagnosed as having ARS resulting from extensive beta radiation burns to the skin and significant whole-body gamma radiation exposure.

The diagnostic criteria used to assess the presence of ARS was the presence, intensity, and duration of symptoms ie, nausea, vomiting, and erythema of the skin and mucosa); time of onset; and the peripheral lymphocyte count, which decreased to less than 10^9/L during the first 24 hours following radiation exposure in patients with ARS. During the first 36 hours after the accident, the 237 hospitalized

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persons were diagnosed as having a clinical pattern consistent with first degree through fourth degree ARS. After admission to the hospital, they were monitored again for contamination and, when necessary, decontaminated with soap, water, and a clothing change. Routine samples of urine and blood were drawn for analysis, and thyroid scanning was performed. The radiation dose received was estimated by counting the number of aberrant chromosomes (dicentrics) in cultured lymphocytes (cytogenetic analysis). The diagnosis of ARS was confirmed during the first five days for persons admitted to the Moscow Hospital. Approximately seven days after the accident, the radiation dose was estimated and the patients were categorized into four groups according to prognosis and severity of hematopoietic syndrome (Table I). Twenty-two injured persons were classified as having fourth degree (extremely severe) ARS; 23 as having third degree (severe) ARS; 53 as having second degree (moderate) ARS; and 139 as having first degree (mild) ARS.[3]

Neutrophil count was used to determine finally the magnitude of radiation dose. The parameter used was the time required for the neutrophils to decrease to 0.5×10^9/L, based on data collected over a period of up to three months in cases that exhibited typical postirradiation platelet and/or neutrophil counts with distinct depletion and restoration phases. Complete blood counts were performed two to three times per week for two to three months. This data was used to definitively confirm the diagnosis and prognosis of ARS. Hyperamylasemia was used as a supplementary diagnostic tool.

Treatment consisted of supportive therapy, which included selective antimicrobial intestinal decontamination, reverse isolation, empiric systemic antibiotic administration, and transfusion replacement of blood and blood products. Definitive treatment of allogeneic bone marrow transplantation (BMT) and human embryonic liver cell transplantation (LCT) was performed on patients with irreversible myelosuppression. A sterile environment was maintained through strict observance of hand washing by all attending personnel upon entering and leaving the room; mandatory use of disposable gowns, masks, and caps; antiseptic decontamination of footwear; changing of patient undergarments daily; antiseptic washing of walls, floors and items used in the room; and individually assigned antiseptically treated nursing items. Isolation rooms provided air sterilization with ultraviolet lamps. The microorganism population was maintained at less than $500\,m^{-3}$ in the room air. Raw fruits and vegetables and canned products were eliminated from the patients' diet.[4]

The decision was made early to perform BMT on patients with third and fourth degree ARS and possible irreversible myelosuppression.[5] These patients vomited within the first half-hour, suffered from diarrhea during the first one to two hours, and from swelling of the parotid gland during the first 24 to 36 hours of exposure, in addition to myelosuppression.

Infections, manifested by the onset of fever and neutropenia, were treated with intravenous administration of triple broad-spectrum antibiotics, including aminoglycoside, cephalosporin and semi-synthetic penicillin. If this regimen did not reduce the fever within 48 hours, three or four doses of gamma globulin were administered. An intravenous antifungal (amphotericin B) was administered if the neutropenic fever persisted for seven days, along with the antibiotics and gamma globulin. Patients with herpes simplex were given acyclovir. Approximately one third of the patients with third and fourth degree ARS had the herpes virus. Viral skin lesions were treated with topical acyclovir. No deaths were attributed to bacterial infection alone in patients with hematopoietic syndrome. However, infectious complication was the primary cause of death in patients with ARS complicated by thermal burns, radiation-induced enteritis, or acute graft-versus-host disease from BMT. The etiology of terminal septicemia, documented by surveillance cultures, was most often from *Staphylococcus epidermidis*.

The hematopoietic syndrome was treated with prophylactic and therapeutic fresh random donor platelets when the platelet count dropped to 20×10^9/L or lower, or with the first sign of bleeding. Transfusions usually were required every one to three days. To inactivate the immunocompetent cells from the donor, all blood components were irradiated with 1,500 cGy of gamma radiation before transfusion. Only one person received single donor platelets. While the majority of patients showed no evidence of overt bleeding, autopsy results disclosed micro-circulatory failure and very porous capillaries in several organs. In some situations, cryo-preserved autologous platelets, as well as allogeneic platelets, were used successfully. Autologous platelets were taken from patients with second and third degree ARS on the first day post-irradiation. Platelet transfusions prevented life-threatening bleeding. Three to eight transfusions of 250 cc per

Table I. Diagnostic Categories for Acute Radiation Sickness (ARS).

Degree of ARS	Dose (cGy)	Severity of ARS	Prognosis
I	100-200	Mild	Very favorable
II	200-400	Moderate	Relatively favorable
III	400-600	Severe	Doubtful
IV	≥ 600	Extremely severe	Poor

person were used to treat patients with second and third degree ARS. No evidence of refractoriness developed. A considerable number of packed red blood cells were transfused in patients with second and third degree ARS accompanied by severe radiation burns.

Allogeneic BMT taken from 113 random related donors was performed on 13 patients with third and fourth degree ARS. Additionally, six patients with fourth degree ARS received embryonic LCT, which contained stem cells and few immunocompetent cells to decrease the risk of developing acute graft-versus-host disease (Table II). Fifty percent (seven patients) of the BMT patients died within 17 days of transplantation (15 to 25 days following radiation exposure) from acute radiation injury to lung, intestine, and/or skin. The remaining six patients did not have severe skin burns or intestinal injuries but received a total radiation dose estimated to be between 440 and 1,020 cGy. Two of the six patients survived BMT (having received 560 cGy and 870 cGy doses, respectively) from haplo-identical female (sisters) donors. Both experienced transient partial engraftment of the transplanted marrow before rejection 32 and 35 days after BMT, respectively, with restoration of their own myelopoiesis after 28 days. These two patients are still alive at more than three and one half years after the accident.[5] A 62-year-old female patient who received LCT lived for 30 days; postmortem findings showed evidence of regeneration of her own myelopoiesis, indicated by female cell karyotype. She had received a male donor transplant.[4,6]

The effectiveness of BMT in an emergency situation may be limited to patients receiving less than 900 cGy of gamma radiation with at least 1% of marrow stem cells remaining, no skin or intestinal radiation injuries, and no combined injury.[7] Seven of the 13 BMT patients died of skin and intestinal injuries before the transplanted marrow engrafted. While recovery of autologous myelopoiesis may occur following large doses of radiation exposures, such as experienced by those patients with third and fourth degree ARS, it is unknown if this occurred due to transient engraftment of transplanted stem cells.

Radiation-induced skin injuries (beta radiation burns) were seen only in combination with hematopoietic syndrome radiation injury. Skin doses of radiation were estimated to be 10 to 20 times greater than bone marrow or whole-body doses, confirming the uncontrolled, nonuniform nature of radiation accident exposure. These skin injuries, according to their severity, duration, and recurrence, contributed significantly to the overall pathophysiology and outcome of the patient. Severe skin injuries were manifested by diffuse hyperemia; secondary erythema; dry and wet desquamation with blistering, ulceration, and necrotic dermatitis; recurrent waves of erythema; and after evidence of healing of the primary lesions, edema, fever, and a worsening of the patient's clinical picture.[4] Topical treatment was necessary, with glucocorticoids and analgesia in the more severe cases. Pain control was relatively ineffective, especially topical anesthesia, which seems to be typical for radiation injuries.

Table II. Transplantation Cases, Estimated Radiation Dose, and Outcome.

Degree of ARS	Dose (cGy)	Treatment	Day of Death	Cause of Death
IV	920	BMT	15	Skin; pneumonitis
IV	1200	BMT	17	Skin; GI injury
IV	1180	BMT	18	Skin; GI injury
IV	1000	BMT	18	Skin; GI injury
III	550	BMT	21	Hemorrhage[1]
IV	830	BMT	24	Pneumonitis
IV	660	BMT	25	ARDS; toxicity
III	440	BMT[2]	34	Mixed infection; GVH
IV	640	BMT[3]	48	Mixed infection; GVH
IV	750	BMT[3]	86	Mixed infection; GVH
IV	1020	BMT[4]	91	Mixed infection; GVH
III	560	BMT[5]	Alive	
IV	870	BMT[5]	Alive	
IV	1110	LCT	14	Skin; GI injury
IV	> 1000	LCT	14	Skin; GI injury
IV	1370	LCT	15	Skin; GI injury
IV	1240	LCT	17	Skin; GI injury
IV	1090	LCT	18	Skin; GI injury
IV	830	LCT[6]	30	Toxicity; ARDS

Note: BMT = bone marrow transplantation; LCT = liver cell transplantation; GI = gastrointestinal injury; GVH = graft-versus-host; ARDS = acute respiratory distress syndrome (respiratory insufficiency).

[1]Hemorrhage from mechanical trauma during catheterization.

[2]BMT from haplo + 1 identical donor but own myelopoiesis restored.

[3]BMT from HLA-identical donor.

[4]BMT from haplo-identical donor but own myelopoiesis restored.

[5]BMT from haplo-identical donor rejected, own myelopoiesis restored.

[6]LCT from male, postmortem evidence of own myelopoiesis being restored.

Burns were fatal in the 19 of 56 patients with radiation burns on > 40% to 100% of body surface area.[6] If early secondary erythema over > 40% body surface area was present, a clinical picture of febrile-toxemia, followed by hepatorenal insufficiency, encephalopathy with cerebral edema, coma, and death resulted 14 to 48 days postirradiation. Plasmapheresis was used to control the hepatorenal insufficiency.[1,4] This treatment prolonged survival slightly but did not prevent death from encephalopathic coma. The burns may have been the primary cause of death in some cases; however, in most cases, the burns were associated with severe hematopoietic syndrome and severe acute gastrointestinal syndrome (enteritis).

In ten patients, the gastrointestinal syndrome was the life-threatening manifestation of ARS, with severe diarrhea suggesting a radiation dose greater than 1,000 cGy. All of these patients died within three weeks of irradiation. When the enteritis persisted in spite of supportive fluid and electrolyte therapy, death may have been caused solely by the gastrointestinal syndrome.

Large amounts of thick rubber-like mucous formed in the oropharyngeal area of about 82 patients and in some cases resulted in respiratory difficulty. Initially, some patients showed benign acute radiation-induced inflammation of cheeks, tongue, and gums. Those having third and fourth degree ARS had, in addition to the rubbery mucous plugs, painful erosions and ulcers of oral mucosa, which required sterile saline irrigation and frequent debridement. In a significant number of patients this radiation-induced inflammation was complicated by secondary bacterical and viral infections.

In one third of the patients with severe hematopoietic syndrome, herpetic lesions formed massive crusts on the lips and face about three to four days postirradiation. Patients with fourth degree ARS and herpetic lesions also developed radiation-induced parotitis, inability to salivate, and resulting hyperamylasemia.[8] No treatment was indicated for the parotitis, which gradually resolved; salivation, however, recurred very slowly.

Rapidly intense dyspnea with acute respiratory insufficiency (adult respiratory distress-like syndrome) was seen in seven patients with third and fourth degree ARS. This condition rapidly progressed for two to three days leading to death. Postmortem examination revealed enlarged blue lungs with interstitial edema but no destruction of mucous membranes of the trachea and bronchi. These patients also had severe skin and intestinal radiation injuries.

Beta radiation caused early damage to the eye tissues; erythema of the eyelid, with increased vasculature of the lid, and conjunctiva. Cutaneous changes were manifested by waves of erythema, hyperpigmentation, and scaling. Partial epilation of the eyebrows was transient, and all patients retained their eyelashes. (Scalp hair growth recovered fully.) Other eye changes noted were decreased corneal sensitivity and superficial radiation-induced keratitis, which regressed over one to two months without corneal opacification. Treatment for the eye changes included topical ointments to the eyelid skin and eyedrops of 20% albucid, sophradex, and vitamin solutions into the conjunctival cavity.[4] One severely ill patient with fourth degree ARS, who survived the acute phase, developed angioretinopathy with hemorrhage and plasma discharges about five months postirradiation. He also had persistent low diastolic pressure in the central retinal artery. He is one of the two surviving BMT patients. No radiation-induced lens changes were observed one year postirradiation.

Convalescence of three to four months was required for those patients with first and second degree ARS; a much longer period was necessary for those having third and fourth degree ARS. The majority of the patients have resumed work but cannot work with radiation sources. Periodic follow-up examinations were made during the first year after the accident. Patients usually had dystrophic and ulcerative skin lesions, some with subcutaneous edema primarily over the knees and feet. Skin lesions were treated with agents that improved local blood circulation and tissue trophism. Five patients suffered deep ulcers which required repeated plastic surgery.

The immunologic status of patients with second, third, and fourth degree ARS, tested 1 to 1.5 years after the accident showed a persistent decrease in T-helper lymphocytes with an increase in T-suppressor lymphocyte activity and a significant decrease in the helper-suppressor ratio. However, there was no evidence of a decrease in the absolute lymphocyte level or in the T- and B-subpopulations. These changes in lymphocyte helper and suppressor populations were not seen in patients with first degree ARS. During the follow-up period, no severe or life-threatening infections were noted. Immunocorrective therapy was attempted using T- and B-activin in several cases. Respiratory infections occurred in three of eight patients with third and fourth degree ARS and only one of 22 patients with second degree ARS. A competent immune system remains critical in enhancing microbial and viral resistance during convalescence of the irradiated patient. A plan of long-term follow-up observation remains in effect.

Conclusion

The consequences of the Chernobyl radiation accident provide data on a large group of critically ill patients who received uniform whole-body irradiation and required treatment of ARS in a massive casualty situation. The event afforded the opportunity to learn many lessons regarding the biomedical effects of ionizing radiation and to clarify many aspects about the early radiobiological effects in humans. The accident also provided data on severe and extensive beta radiation skin injuries, which com-

plicated the course of illness and played a significant role in the death of 19 of the 31 patients. Combined injuries consisting of trauma, thermal burns, and radiation were the cause of death in two patients very early in the course of ARS. Clinical ARS was observed in man, the degrees of severity defined according to average radiation dose exposure, and prognosis made for the course of ARS based on biological criteria. Information for biological dosimetry was obtained from karyotypical analysis, lymphocyte counts, and symptoms during the early stages of illness; later the granulocyte count proved to be a useful dosimetric tool. While continuous data and follow-up assessment is necessary, this information should prove useful in responding to radiation accidents and providing effective medical care to the resulting casualties.

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